No. 5,374,242 issued December 20, 1994; U.S. No. 5,498,235 issued March 12, 1996; U.S. No. 5,730,716 issued March 24, 1998; U.S. No. 6,001,088 issued December 14, 1999; U.S. No. 6,018,679 issued January 25, 2000; U.S. No. 6,139,537 issued October 31, 2000; U.S. No. 6,148,231 issued November 14, 2000; U.S. No. 6,154,671 issued November 28, 2000 and U.S. No. 6,167,302 issued December 26, 2000, documents which are herein incorporated by reference.--

In the Claims:

Kindly replace claims 20 and 21 as follows:

20. (Amended) The method of claim 1 wherein the iontophoresis system used in step b) is a device selected from the group consisting of:

(A) a device comprising a constant current source; applicator and grounding electrodes for emplacement upon patient tissue to provide a current path therethrough for performing iontophoresis upon a portion of said tissue, electrically connection between said current source and said electrodes to thereby produce a voltage differential across said electrodes, an impedance checking circuit coupled to said electrodes and capable of setting predetermined limits of impedance as measured across said electrodes which mark the bounds of safe operation for said device, said impedance checking circuit also capable of signaling the occurrence of impedance values outside these predetermined limits, a safety-shutdown circuit coupled to said impedance checking circuit and capable of responding to said impedance

value signal for preventing current flow and voltage differential across said electrodes;

(B) a device comprising a pouch for holding a fluid containing the chemical species, said pouch including flexible and deformable walls adapted to generally conform to surface shapes against which they are placed, at least a portion of which includes a microporous membrane separating the interior of the pouch from the exterior and having openings of about 0.22 microns or less in diameter, said portion being formed to present a generally planar to convex exterior surface, and an electrode carried by said pouch for coupling to an electric potential source, and optionally further comprising a second pouch for holding a fluid containing additional chemical species, said second pouch including flexible and deformable walls adapted to generally conform to surface shapes against which they are placed, at least a portion of which includes a microporous membrane separating the interior of the second pouch from theexterior and having openings of about 0.22 microns or less in diameter, said portion of said second pouch being formed to present a generally planar to convex exterior surface, a second electrode carried by said second pouch for coupling to an electric potential source, and flexible coupling between the first-mentioned and second pouch;

B3 cont'd

(C) a device which performs a method of minimizing vesicle formation while applying iontophoretic treatment to a living body, said method including the steps of: conducting direct current through the skin of

said body in a first direction from a first electrode to a second electrode on said skin, intermittently reversing the polarity of said electrodes to cause direct current to flow in a second direction opposite said first direction, and controlling the flow of said current in said first and second directions so that the energy applied in said first direction exceeds the energy applied in said second direction by a ratio of between about 2:1 and 7:1;

B3 cont'd

(D) a device for performing a method of iontophoretic drug delivery wherein an electrochemically active component of either the anode or the cathode of the iontophoresis device is intentionally comprised of a material that effects oxidation/reduction without being consumed to produce a species which interacts with an intentionally selected drug in which a corresponding weak acid/weak base form is selected to be delivered, so that water hydrolysis products are minimized;

(E) a device comprising an aqueous medicament solution including medicament ions and complementary ions, said complementary ions being chloride ions, a first electrode constructed of silver which is capable of reacting with the complementary chloride ion to form silver chloride which is insoluble in the medicament solution, an arrangement capable of placing the first electrode in communication with the aqueous medicament solution, an arrangement capable of placing the aqueous medicament solution in communication with a patient, means for placing a second electrode in communication with a patient at a point on said patient

separated from said first electrode, and an arrangement capable of applying an electrical voltage difference between the first and second electrodes such that the medicament ions are transported to the patient, and such that the first electrode reacts with the complementary ions at a voltage below the electrolysis voltage of water;

B3 cont'd

(F) a device for performing a method comprising the steps of obtaining an ion exchange matrix and a drug comprising medicament ions which are insoluble in an iontophoresis medium and complementary ions, obtaining a first electrode and a second electrode, obtaining an iontophoresis medium, placing the ion exchange matrix and the drug in communication with iontophoresis medium such that the medicament ions are precipitated onto the ion exchange matrix, placing the first electrode in communication with the iontophoresis medium, placing the iontophoresis medium in communication with the patient such that the medium is disposed between the first electrode and the skin of the patient, placing the second electrode in communication with the skin of the patient at a point distal from the first electrode, and creating an electrical voltage difference between the first and second electrodes, said voltage difference causing the electrolysis reaction of water, the products

of the electrolysis of water acting to solubilize the medicament such that the medicament ions are transported through the skin of the patient, while an approximately constant pH is maintained within the iontophoresis medium;

(G) a device comprising a housing for said electrode, a first chamber which contains an electrolytic solution to permit said iontotherapeutic delivery to take place and having present therein ion exchange granules which inhibit increased ionic content through ion generation in the electrode in the first chamber as the iontotherapeutic process takes place, an electrical terminus to contact electrically the electrolytic solution contained in said first chamber, a second chamber for receiving a unit dose of said ionized pharmaceutical, and a permselective membrane separating said first and second chambers, said membrane characterized by having pores with sufficiently low permeability to inhibit substantial passage of said ionized pharmaceutical present in said second chamber into said first chamber, said permselective membrane being substantially free of ion exchange sites;

B3 cont'd

(H) a device comprising a first electrode for containing a beneficial agent to be delivered and for contacting a body surface of a patient in agent-transmitting relation therewith, a second electrode for contacting the body surface in ion-transmitting relation therewith at a location spaced apart from the first electrode, first and second electrical power sources, each having a pair of terminals and each producing an electrical potential difference between its said pair of terminals; and bi-state switch, coupled to said two power sources and said first and second electrode, for selectively switching between: (1) a first state, in which said

two power sources are connected in series circuit relation between said first and second electrodes, and (2) a second state, in which said two power sources are connected in parallel circuit relation between said first and second electrode, where switching occurs in response to a change of electrical resistance of the patient's body surface;

B3 cont'd

(I) a device comprising a medicament-containing disposable patch removably positionable on the skin of a patient for permitting iontophoretic delivery of medicament transcutaneously, a controller including electronic components for electrically controlling said medicament delivery, the patch including a flexible planar patch body having a medicament-containing first surface, an opposed second surface and an extending planar tab for insertable electrical accommodation in said controller, said first surface of said planar patch body being supportable on the skin of said patient, said opposed second surface of said patch body and said controller including co-operative removable fastening arrangement capable of removably fastening said controller to said patch and for maintaining said controller in a fastened condition with respect to said patch with said tab electrically accommodated in said controller;

(J) a device comprising an electrical power source for supplying an electrical current, an electronic controller for controlling the supply of electrical current, a first electrical current distribution element associated with the first side of the electrical power source and a second electrical

current distribution element associated with the second side of the electrical power source, a first hydratable matrix element associated with the first electrical current distribution element and a second hydratable matrix element associated with the second current distribution element, first and second hydration means associated, respectively, with the first and second hydratable matrix elements for hydrating said matrix elements, each of said hydration means including a hydration assembly comprising a hydrating liquid, a releasably sealed liquid-storage component comprising a first portion releasably sealed to a strip element to define said releasably sealed liquid-storage component therebetween, and an extending tab member, said extending tab member being continuous with a first end of said strip element, wherein said releasably sealed liquid-storage component contains the hydrating liquid and is disposed with respect to the associated hydratable matrix such that operation of the tab member causes progressive unsealing of the releasable seal that seals the liquid-storage component and causes progressive deposit of the hydrating liquid upon said matrix element;

B3 cont'd

(K) a device for performing a method comprising the steps of inserting a first electrode into a nasal passage of a subject and applying a second electrode to the subject adjacent the eye or adjacent the ear wherein said first and second electrodes are each electrically connected to a power source and said target tissue is sandwiched between each of said electrodes to achieve a current path which is of minimal electrical resistance and

delivering said composition comprising said chimeric oligonucleotide to said target tissue, wherein the first electrode is a donor electrode and the second electrode is a receptor electrode and wherein the donor electrode is a needle electrode and wherein the donor electrode is a pad for topical administration and wherein the donor electrode includes an electrode body formed from insulating material, a conductor passing through the electrode body and a compartment for storage of the composition comprising said chimeric oligonucleotide located adjacent an outer end of the electrode body;

B3 cont'd

(L) a device for performing a method comprising applying a transdermal patch to the skin of a living body, causing current to flow through the skin so as to iontophoretically deliver a bisphosphonate compound wherein said compound causes delayed onset of local skin irritation, and reversing the direction of current flow through the skin for a reversal period of long enough duration to reduce the effects arising from the delayed onset of local skin irritation caused by the compound;

(M) a device comprising a medicament-dispensing applicator electrode for use with an electrokinetic device to transdermally deliver a medicament to an individual, comprising a substrate having a first surface and a second surface opposite said first surface, said substrate including a medicament-dispensing portion comprising a cell or a plurality of cells forming an aperture or a plurality of apertures between said first surface and said second surface, said cell or plurality of cells containing the medicament,

and a layer of adhesive covering at least a portion of said second surface of said substrate opposite said first surface for releasably attaching said substrate to an electrokinetic device containing an electrical power source for electrokinetically driving said medicament through said first surface and into the individual's skin upon application of an electrical current to effect delivery of said medicament in said cell or plurality of cells to the individual's skin;

B3 cont'd

(N) a device comprising a reservoir configured to receive the composition comprising said chimeric oligonucleotide and having an internal wall, an external wall, and an end wall bridging the internal wall and the external wall, the internal wall and the external wall being annular and having a free end configured to be applied to an eyeball, said device further comprising at least one active electrode arranged in the reservoir, a passive electrode and a current generator, wherein the at least one active electrode is a surface electrode arranged on an interior surface of the end wall and wherein the internal wall has an outer diameter that is configured to be at least equal to a predetermined diameter, whereby the predetermined diameter represents a diameter of a human cornea; and

(O) a device comprising at least a set of electrodes including an electrode joined to a reservoir that can be charged with the composition comprising said chimeric oligonucleotide and a counter-electrode, an electronic module separably mounted on said set of electrodes to control a

therapeutic electric current flowing, between the two electrodes through the reservoir and the skin of a patient applied against said reservoir, said electronic module comprising an arrangement capable of controlling the operation of the device, said device further comprising an electronic key including a memory loaded with a predetermined code, a cradle to temporarily receive said module and an arrangement capable of establishing electrical connections to said module to read this code by reading means present in the module, said control means of said module being responsive to the code of said key to selectively authorize the operation of the device.

B3 cont'd

21. (Amended) The method of claim 20, wherein the iontophoresis system used in step b) is a device comprising a reservoir configured to receive the composition comprising said chimeric oligonucleotide and having an internal wall, an external wall, and an end wall bridging the internal wall and the external wall, the internal wall and the external wall being annular and having a free end configured to be applied to an eyeball, said device further comprising at least one active electrode arranged in the reservoir, a passive electrode and a current generator, wherein the at least one active electrode is a surface electrode arranged on an interior surface of the end wall and wherein the internal wall has an outer diameter that is configured to be at least equal to a predetermined diameter, whereby the predetermined diameter represents a diameter of a human cornea.